17e JOURNÉE SCIENTIFIQUE DU GRPSO ET DU GREAT

Groupe de **R**echerche sur le **PSO**riasis

Groupe de **R**echerche sur l'**E**czéma **AT**opique
DA (Dermatite Atopique)

VENDREDI
6 OCTOBRE
2023

ESPACE DU CENTENAIRE
Maison de la RATP - Paris

GRPso
Groupe de Recherche sur le Psoriasis

great
GROUPE DE RECHERCHE SUR L'ECZÉMA ATOPIQUE

Sous l'égide de la
Société Française de Dermatologie et de Pathologie Sexuellement Transmissible

17e JOURNÉE SCIENTIFIQUE DU GRPSO ET DU GREAT
Groupe de Recherche sur le PSOriasis
Groupe de Recherche sur l'Eczéma ATopique
DA (Dermatite Atopique)

VENDREDI 6 OCTOBRE 2023
ESPACE DU CENTENAIRE
Maison de la RATP - Paris

Quoi de neuf dans le traitement de la DA en 2023?

Pr Manuelle Viguier

Hôpital Robert Debré, CHU de Reims

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Sous l'égide de la
Société Française de Dermatologie

Liens d'intérêt

Sur les 3 dernières années:

- Recherches cliniques : Boehringer Ingelheim, Léo Pharma
- Advisory Boards : Janssen-Cilag, Lilly, Novartis, Abbvie, Boehringer Ingelheim, Bristol Myers Squibb, Léo Pharma, Nordic Pharma
- Cours, formations : Amgen, Médac, Abbvie, Almirall
- Aides pour des recherches : Janssen-Cilag

Traitements systémiques de la dermatite atopique en 2023 (AMM + remboursement)

Ciclosporine	Dupilumab (Dupixent®) (anti IL-4/IL-13)	Tralokinumab (Adtralza®) (anti IL-13)	Baricitinib (Olumiant®) (anti JAK1/JAK2)	Upadacitinib (Rinvoq®) (anti JAK1)	Abrocitinib (Cibinqo®) (anti JAK1)
Formes sévères de DA de l'adulte, en cas d'inefficacité, d'intolérance ou de contre-indications des traitements classiques (photothérapie et/ou photochimiothérapie). **Ciclosporine non recommandée par l'AMM chez les patients de moins de 16 ans**	**DA modérée à sévère** de l'**enfant de 6 mois à 11 ans et de l'adolescent âgé de 12 ans et plus** qui nécessitent un traitement systémique (échec DC) **Dermatite atopique modérée à sévère** de l'**adulte** qui nécessite un traitement systémique en cas d'échec, d'intolérance ou de contre-indication à la ciclosporine	**DA modérée à sévère** de l'**adulte** qui nécessite un traitement systémique en cas d'échec, d'intolérance ou de contre-indication à la ciclosporine	**DA modérée à sévère** de l'**adulte** qui nécessite un traitement systémique en cas d'échec, d'intolérance ou de contre-indication à la ciclosporine	**Dermatite atopique modérée à sévère** de **l'adolescent âgé de 12 ans et plus** qui nécessitent un traitement systémique (échec DC) **DA modérée à sévère** de l'**adulte** qui nécessite un traitement systémique en cas d'échec, d'intolérance ou de contre-indication à la ciclosporine	**DA modérée à sévère** de l'**adulte** qui nécessite un traitement systémique en cas d'échec, d'intolérance ou de contre-indication à la ciclosporine
	200 mg, 300 mg, stylo, seringue	150 mg	2 mg*, 4 mg*	15 mg**, 30 mg, (45 mg)	50 mg*, 100 mg*, 200 mg*
	600 mg puis 300 mg/2s	600 mg puis 300 mg/2s	2 ou 4 mg/j	15 ou 30 mg/j	100 ou 200 mg/j
	Asthme à partir de 6 ans Polypose nasosinusienne Oesophagite à éosinophiles (Prurigo nodulaire)	Pas autre indication	PR Arthrite chronique juvénile (Pelade)	PR Rhum pso SPA (RCH, maladie de Crohn)	Pas autre indication

*: prix identique quelque soit dose unitaire
**: prix adapté à la posologie

GUIDELINE

European guideline (EuroGuiDerm) on atopic eczema: part I – systemic therapy

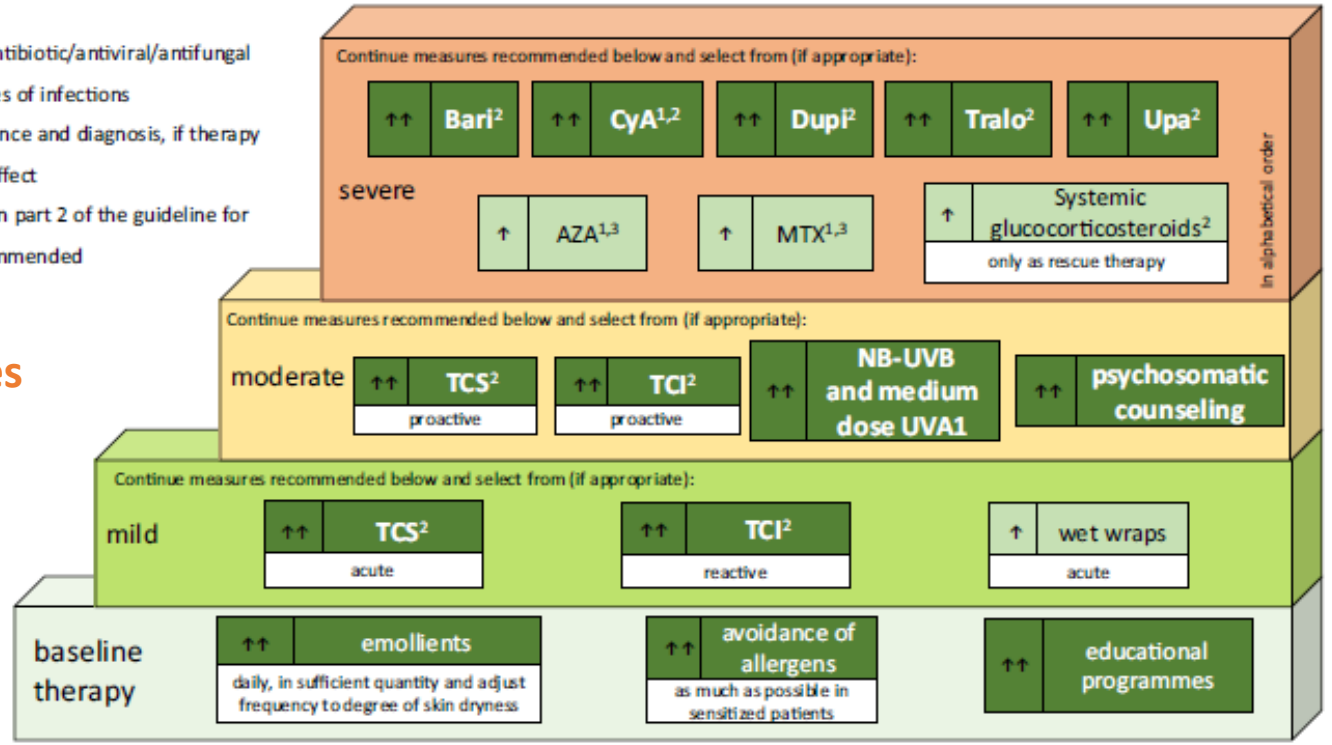
A. Wollenberg,[1,2,*] M. Kinberger,[3] B. Arents,[4] N. Aszodi,[1] G. Avila Valle,[3] S. Barbarot,[5] T. Bieber,[6] H.A. Brough,[7,8] P. Calzavara Pinton,[9] S. Christen-Zäch,[10] M. Deleuran,[11] M. Dittmann,[3] C. Dressler,[3] A.H. Fink-Wagner,[12] N. Fosse,[13] K. Gáspár,[14] L. Gerbens,[15] U. Gieler,[16] G. Girolomoni,[17] S. Gregoriou,[18] C.G. Mortz,[19] A. Nast,[3] U. Nygaard,[20] M. Redding,[21] E.M. Rehbinder,[22] J. Ring,[23] M. Rossi,[24] E. Serra-Baldrich,[25] D. Simon,[26] Z.Z. Szalai,[27] J.C. Szepietowski,[28] A. Torrelo,[29] T. Werfel,[30] C. Flohr[31,32,*]

JEADV 2022, 36, 1409–1431

Un positionnement identique de ces différentes molécules dans les dernières recommandations (2022)

Stepped-care plan for adults with atopic eczema

- Add antiseptic/antibiotic/antiviral/antifungal treatment in cases of infections
- Consider compliance and diagnosis, if therapy has insufficient effect
- Refer to Table 2 in part 2 of the guideline for TCS classes recommended



[1] refer to guideline text for restrictions, [2] licensed indication, [3] off-label treatment
↑↑ (dark green) strong recommendation for the use of an intervention / ↑ (light green) weak recommendation for the use of an intervention
For definitions of disease severity, acute, reactive, proactive see section 'VII' and section 'Introduction to systemic treatment' of the EuroGuiDerm Atopic Eczema Guideline
Abro=abrocitinib; AZA=azathioprine; Bari=baricitinib; CyA=ciclosporin; Dupi=dupilumab; MTX=methotrexate; TCI=topical calcineurin inhibitors; TCS= topical corticosteroids; Tralo=tralokinumab; Upa=upadacitinib; UVA1=ultraviolet A1; NB-UVB=narrow-band ultraviolet B

100% Agreement

Symbols	Implications (adapted from GRADE [1])
↑↑	We believe that all or almost all informed people would make that choice.
↑	We believe that most informed people would make that choice, but a substantial number would not.
0	We cannot make a recommendation.
↓	We believe that most informed people would make a choice against that intervention, but a substantial number would not.
↓↓	We believe that all or almost all informed people would make a choice against that choice.
	No recommendation.

Figure 1 Stepped-care plan for adults with AE.

Une efficacité cependant différente

Dermatol Ther (Heidelb)
https://doi.org/10.1007/s13555-023-01000-3

ORIGINAL RESEARCH

Comparative Efficacy of Targeted Systemic Therapies for Moderate-to-Severe Atopic Dermatitis without Topical Corticosteroids: An Updated Network Meta-analysis

Jonathan I. Silverberg · H. Chih-ho Hong · Brian M. Calimlim · Wan-Ju Lee · Henrique D. Teixeira · Eric B. Collins · Marjorie M. Crowell · Scott J. Johnson · April W. Armstrong

Received: June 2, 2023 / Accepted: August 2, 2023

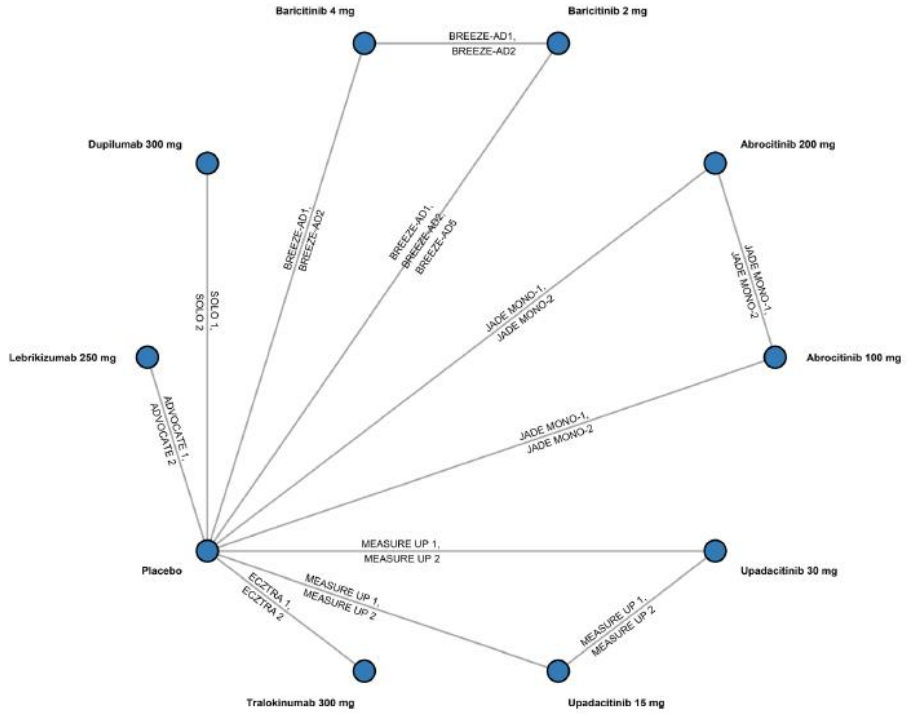


Fig. 1 Network meta-analysis diagram. Network displayed above is for primary endpoint analysis. The ΔNRS ≥ 4 network of the week 2 analysis is identical to the above except without ECZTRA 1 and ECZTRA 2 (tralokinumab) as these trials did not report ΔNRS ≥ 4 at week 2. The EASI-75 network of the week 2 analysis is identical except with pooled SOLO 1 and SOLO 2 data as reported in Thaçi et al. [18]. *EASI* Eczema Area and Severity Index, *EASI-75* EASI improvement ≥ 75% from baseline, *NRS* Numerical Rating Scale, *ΔNRS ≥ 4* Pruritus Numerical Rating Scale reduction of ≥ 4 points from baseline

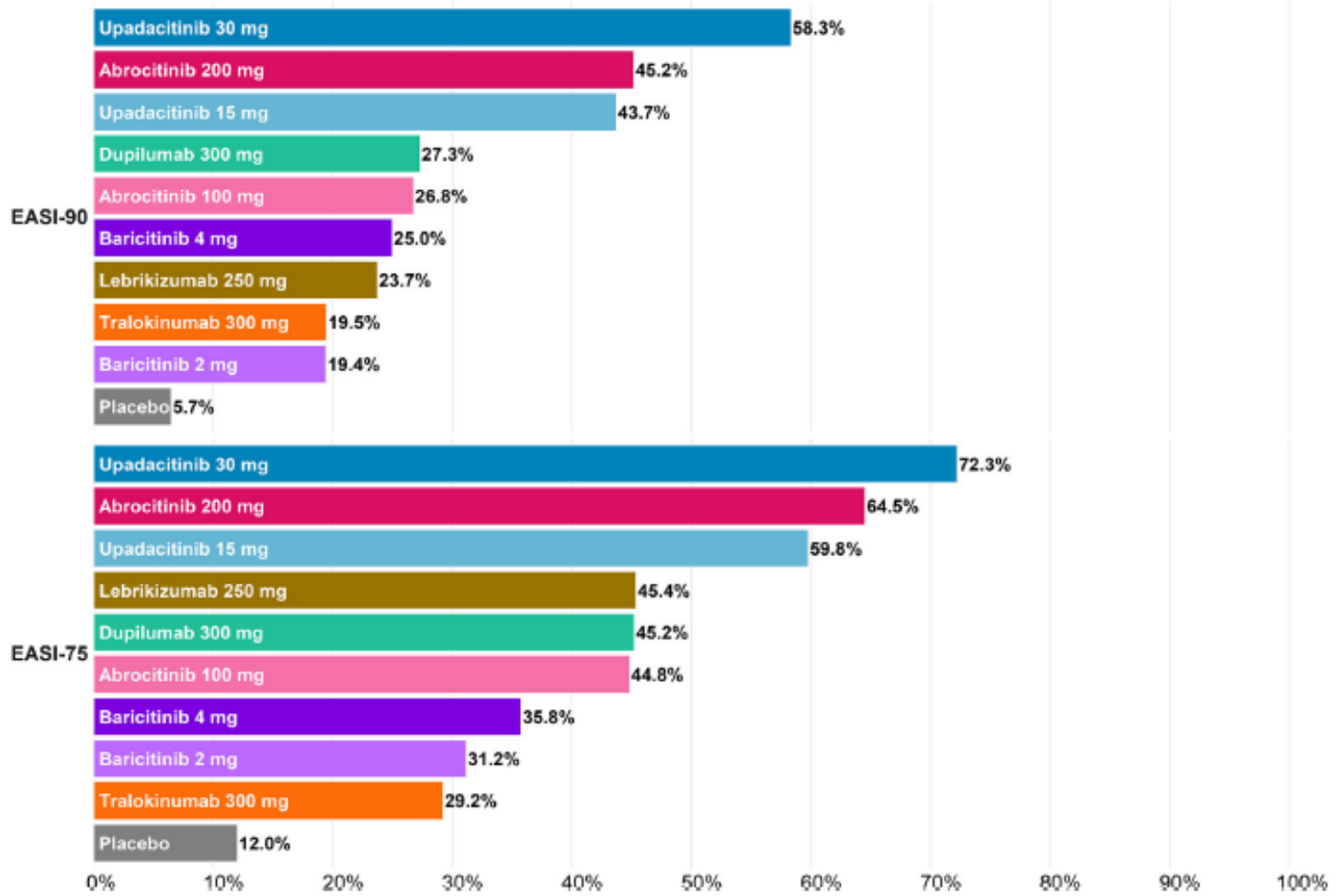


Fig. 2 EASI-75 and EASI-90 absolute response rate estimates for moderate-to-severe atopic dermatitis (primary endpoint timepoint). *EASI* Eczema Area and Severity Index, *EASI-75* EASI improvement ≥ 75% from baseline, *EASI-90* improvement ≥ 90% from baseline

life

MDPI

Systematic Review

Short-Term Effectiveness and Safety of Biologics and Small Molecule Drugs for Moderate to Severe Atopic Dermatitis: A Systematic Review and Network Meta-Analysis

José-Juan Pereyra-Rodriguez [1,2,*], Sara Alcantara-Luna [3], Javier Domínguez-Cruz [1], Manuel Galán-Gutiérrez [4], Ricardo Ruiz-Villaverde [5], Samuel Vilar-Palomo [6] and Jose-Carlos Armario-Hita [7]

Life **2021**, *11*, 927. https://doi.org/10.3390/life11090927

SYSTEMATIC REVIEW

Comparative efficacy and safety of systemic therapies used in moderate-to-severe atopic dermatitis: a systematic literature review and network meta-analysis

J.I. Silverberg,[1] J.P. Thyssen,[2] K. Fahrbach,[3] K. Mickle,[3] J.C. Cappelleri,[4] W. Romero,[5] M.C. Cameron,[6,a] D.E. Myers,[7] C. Clibborn,[5] M. DiBonaventura[6,*]

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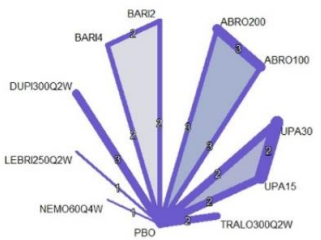
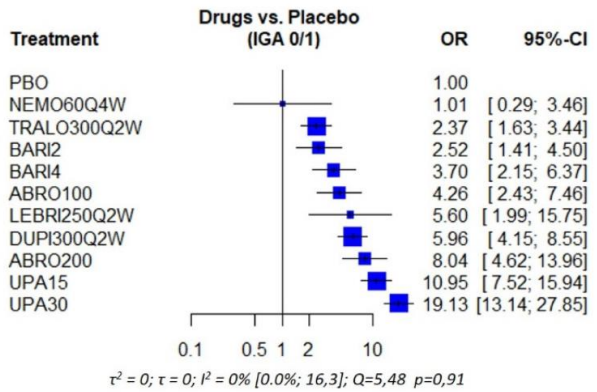
[2]Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark
[3]Evidera Inc, Waltham, MA, USA
[4]Pfizer Inc, Groton, CT, USA
[5]Pfizer Ltd, Surrey, UK
[6]Pfizer Inc, New York, NY, USA
[7]Pfizer Inc, Collegeville, PA, USA
*Correspondence: M. DiBonaventura. E-mail: marco.dibonaventura@pfizer.com

JEADV 2021, **35**, 1797–1810

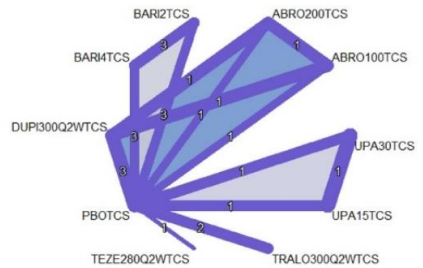
IGA 0 ou 1, sans (a) et avec (b) corticothérapie locale

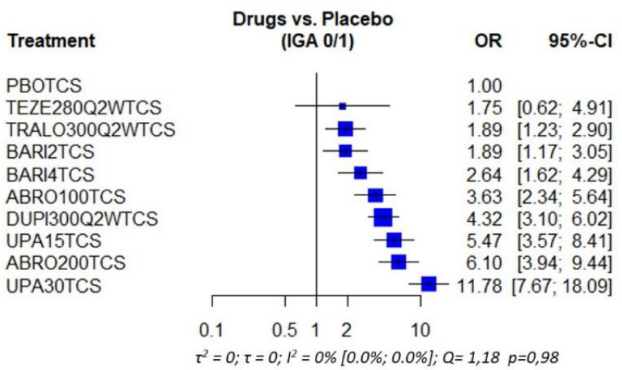
(a)





(b)





Données nouvelles sur les profils de tolérance

Anti JAK

Received: 14 March 2023 | Accepted: 18 July 2023
DOI: 10.1111/jdv.19426

SYSTEMATIC REVIEW

The safety of systemic Janus kinase inhibitors in atopic dermatitis: A systematic review and meta-analysis of randomized controlled trials

Sanghyuk Yoon[1] | Kihun Kim[1,2] | Kihyuk Shin[3,4,5] | Hoon-Soo Kim[3] | Byungsoo Kim[3] | Moon-Bum Kim[3] | Hyun-Chang Ko[3,4,5] | Yun Hak Kim[1,2]

14 essais contrôlés des 3 principaux anti JAK contre placebo (2019-2022)
Etude de 11 effets secondaires d'intérêt

TABLE 1 Characteristics of included studies.

Author, year	Study design	No. of subjects	Study duration (weeks)	Exposure
Bieber 2021 (JADE compare)[38]	Phase 3, randomized, double-blind, double-dummy, placebo-controlled, parallel group, multicentre study	595	16	Abrocitinib 100 mg QD; abrocitinib 200 mg QD; placebo
Bieber 2022[39]	Phase 3, multicentre, double-blind, randomized, placebo-controlled study	463	52	Baricitinib 1 mg QD; baricitinib 2 mg QD; baricitinib 4 mg QD; placebo
Eichenfield 2021[40]	Phase 3, multicentre, international, randomized, placebo-controlled, parallel-group study	285	12	Abrocitinib 100 mg QD; abrocitinib 200 mg QD; placebo
Gooderham 2019[41]	Phase 2b, multicentre, randomized, double-blinded, placebo-controlled, parallel-group study	267	12	Abrocitinib 10 mg QD; abrocitinib 30 mg QD; abrocitinib 100 mg QD; abrocitinib 200 mg QD; Placebo
Guttman-Yassky 2019[42]	Phase 2, parallel, double-blinded, randomized placebo-controlled multiple-dose study	124	16	Baricitinib 2 mg QD; baricitinib 4 mg QD; placebo
Guttman-Yassky 2020[43]	Phase 2b, double-blind, randomized, parallel-group, dose-ranging study	167	16	Upadacitinib 7.5 mg QD; upadacitinib 15 mg QD; upadacitinib 30 mg QD; placebo
Guttman-Yassky 2021 (Measure Up 1)[44]	Phase 3, multicentre, randomized, double-blind, placebo-controlled study	847	16	Upadacitinib 15 mg QD; upadacitinib 30 mg QD; placebo
Guttman-Yassky 2021 (Measure Up 2)[44]	Phase 3, multicentre, randomized, double-blind, placebo-controlled study	836	16	Upadacitinib 15 mg QD; upadacitinib 30 mg QD; placebo
Katoh 2021[45]	Phase 3, randomized, double-blind, multicentre study	272	16	Upadacitinib 15 mg QD; upadacitinib 30 mg QD; placebo
Reich 2020[46]	Phase 3, multicentre, double-blind, placebo-controlled, parallel arm, randomized clinical study	329	16	Baricitinib 2 mg QD; baricitinib 4 mg QD; placebo
Reich 2021[47]	Phase 3, randomized, double-blind, placebo-controlled study	901	16	Upadacitinib 15 mg QD; upadacitinib 30 mg QD; placebo
Silverberg 2020[48]	Phase 3, multicentre, international, placebo-controlled, parallel-group randomized clinical study	391	12	Abrocitinib 100 mg QD; abrocitinib 200 mg QD; placebo
Simpson 2020[49]	Phase 3, multicentre, double-blind, randomized, placebo-controlled study	387	12	Abrocitinib 100 mg QD; abrocitinib 200 mg QD; placebo
Simpson (2) 2020 (BREEZE-AD1)[50]	Phase 3, independent randomized, double-blind, parallel-group, placebo-controlled study	624	16	Baricitinib 1 mg QD; baricitinib 2 mg QD; baricitinib 4 mg QD; placebo
Simpson (2) 2020 (BREEZE-AD2)[50]	Phase 3, independent randomized, double-blind, parallel-group, placebo-controlled study	615	16	Baricitinib 1 mg QD; baricitinib 2 mg QD; baricitinib 4 mg QD; placebo
Simpson 2021[51]	Phase 3, randomized, double-blinded, parallel-controlled study	440	16	Baricitinib 1 mg QD; baricitinib 2 mg QD; placebo

Risque augmenté par rapport au placebo:
HSV
Céphalées
Nausées
Acné
Augmentation CPK

TABLE 2 Risk of adverse events according to the type of JAK inhibitor used in patients with atopic dermatitis.

Jak inhibitor type	Number of results (*n*)	No of subjects	Heterogeneity (%)[a]	Relative risk (95% confidence interval)[b]
Serious infection				
Baricitinib	3	1229	19	0.65 (0.16–2.74)
Abrocitinib	3	1229	0	0.94 (0.15–5.72)
Upadacitinib	5	3021	0	0.95 (0.36–2.54)
Herpes zoster				
Baricitinib	5	2591	0	1.77 (0.47–6.64)
Abrocitinib	5	1925	0	1.64 (0.42–6.39)
Upadacitinib	5	3021	0	2.23 (0.91–5.47)
NMSC				
Baricitinib	5	2467	Not applicable	0.25 (0.02–3.98)
Abrocitinib	4	1658	Not applicable	0.85 (0.03–20.78)
Upadacitinib	5	3021	0	1.81 (0.29–11.06)
Malignancies other than NMSC				
Baricitinib	5	2467	0	0.11 (0.01–0.97)
Abrocitinib	4	1658	Not applicable	Not estimable
Upadacitinib	5	3021	0	1.81 (0.29–11.06)
MACE				
Baricitinib	5	2467	Not applicable	0.76 (0.03–18.51)
Abrocitinib	4	1658	Not applicable	Not estimable
Upadacitinib	5	3021	Not applicable	1.49 (0.06–36.26)
VTE				
Baricitinib	5	2467	Not applicable	1.48 (0.06–36.02)
Abrocitinib	5	1925	Not applicable	Not estimable
Upadacitinib	5	3021	Not applicable	0.17 (0.01–4.07)
Headache				
Baricitinib	5	2263	38	1.68 (0.96–2.94)
Abrocitinib	5	1925	0	1.47 (0.90–2.42)
Upadacitinib	4	2749	0	1.34 (0.93–1.92)
Nasopharyngitis				
Baricitinib	6	2591	38	1.05 (0.76–1.14)
Abrocitinib	4	1658	0	1.19 (0.81–1.74)
Upadacitinib	5	3021	0	1.25 (0.97–1.60)
Acne				
Baricitinib	1	328	Not applicable	2.45 (0.29–20.75)
Abrocitinib	4	1658	0	5.15 (1.43–18.57)
Upadacitinib	5	3021	0	5.08 (3.37–7.67)
Blood creatinine phosphokinase elevation				
Baricitinib	6	2578	0	1.69 (1.22–2.34)
Abrocitinib	3	1063	15	2.14 (0.54–8.51)
Upadacitinib	5	3021	0	2.10 (1.33–3.34)
Nausea				
Baricitinib	1	438	Not applicable	1.33 (0.36–4.95)
Abrocitinib	5	1925	0	5.35 (2.65–10.80)
Upadacitinib	1	166	Not applicable	2.22 (0.28–17.52)

Pas de risque augmenté par rapport au placebo:

Infections sévères

Cancers cutanés (hors mélanome)

Cancer non cutanés

MACE

Manifestations thrombo-emboliques

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Malignancies other than NMSC				
Baricitinib	5	2467	0	0.11 (0.01–0.97)
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MACE				
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Headache				
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Blood creatinine phosphokinase elevation				
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Nausea				
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Abrocitinib	5	1925	0	5.35 (2.65–10.80)
Upadacitinib	1	166	Not applicable	2.22 (0.28–17.52)

Avis publié le 4 novembre 2022 par le comité de pharmacovigilance (PRAC) de l'Agence européenne des médicaments (EMA)

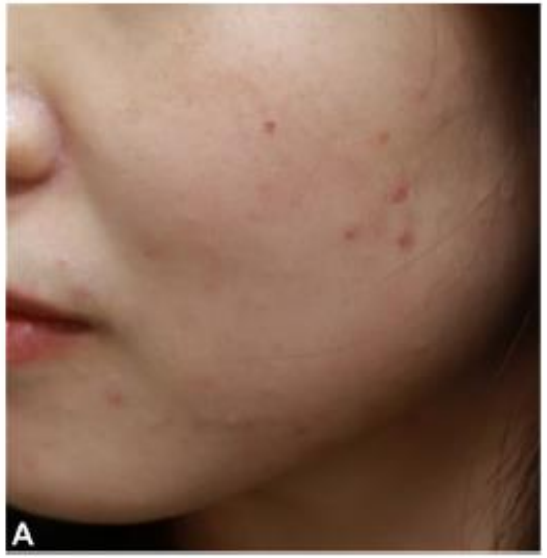
- **Inhibiteurs de JAK utilisés dans les maladies inflammatoires chroniques : recommandations pour réduire le risque d'effets secondaires graves** (troubles cardiovasculaires, caillots sanguins, infections graves, cancers) associés aux inhibiteurs de Janus Kinase (JAK)

  Ces médicaments ne soient utilisés qu'en l'absence d'alternative thérapeutique appropriée chez les patients :
  - Âgés de plus de 65 ans
  - Avec des facteurs de risque d'évènements cardiovasculaires majeurs (tels qu'une crise cardiaque ou un accident vasculaire cérébral)
  - Avec des facteurs de risque de cancer
  - Présentant un tabagisme (présent ou passé)
- **Les inhibiteurs de JAK soient utilisés avec prudence** chez les patients présentant des facteurs de risque de caillots sanguins dans les poumons et dans les veines profondes (risque de thromboembolie veineuse) ;
- **La posologie soit réduite** pour certains groupes de patients présentant un risque de thromboembolie veineuse, de cancer ou d'évènements cardiovasculaires majeurs.
- Les inhibiteurs de JAK concernés sont les suivants : baricitinib/ tofacitinib/ upadacitinib/filgotinib/abrocitinib.

Review > Inflamm Res. 2023 Sep;72(9):1861-1871. doi: 10.1007/s00011-023-01789-x.
Epub 2023 Sep 14.

Association of risk of incident acne and treatment with systemic Janus kinase inhibitors in atopic dermatitis: a systematic review and meta-analysis

Chen Sun [1], Zheng Su [1], Yue-Ping Zeng [2]



Lee SD, et al. JAAD Case reports 2022

RCT Abrocitinib (n=5), upadacitinib (n=4), baricitinib (n=1)

Contrôles: placebo ou dupilumab

7901 patients

Molécule	Mantel-Haenszel risk difference; IC95%, p
Abrocitinib 200 mg	3,69; 1,60-8,48, p<0,01
Upadacitinib 15 mg	4,61; 2,79-7,62, p<0,00001
Upadacitinib 30 mg	6,82; 4,59-10,13, p<0,00001

Pas de risque significatif par rapport aux contrôles pour baricitinib (2 ou 4 mg) ou abrocitinib 100 mg

Données nouvelles sur les profils de tolérance

Dupilumab

Received: 3 January 2023 | Accepted: 20 February 2023
DOI: 10.1111/1346-8138.16764

ORIGINAL ARTICLE

The Journal of Dermatology

Dupilumab-associated cutaneous adverse events among adult patients with atopic dermatitis: A retrospective study

Maddalena Napolitano[1] | Gabriella Fabbrocini[1] | Cataldo Patruno[2]

Etude rétrospective napolitaine sur 916 patients avec DA ayant reçu au moins 1 mois de dupilumab (2018-2022)

Durée moyenne traitement par dupilumab: 27.31+/-21.26 mois

148 patients (16% de la cohorte) ont développé au moins 1 effet secondaire cutané

TABLE 2 Data on cAEs in 148 among 916 (16.15%) patients treated with dupilumab.

cAEs	*n* (%)	Mean dupilumab treatment duration at onset of cAEs	Management, *n* (%)	Dupilumab discontinuation, *n* (%)
HN-D	73 (7.96)	4.14 ± 3.72	TT: 38 (52.05) TCs: 27 (36.98) TT + TCs: 5 (6.85) TA: 3 (4.10) SCs: 12 (16.43) SA: 5 (6.85)	18 (24.65) Preexistent HN-D: 10 (13.7) New-onset HN-D: 8 (10.95)
ACD	6 (0.65)	8.22 ± 2.12	Allergens avoidance	0 (0)
AIFF	3 (0.32)	6.13 ± 2.15	–	0 (0)
Psoriasis	39 (4.25)	5.39 ± 1.42	TCs: 26 (66.67) nb-UVB: 11 (28.2) Methotrexate: 2 (5.13)	10 (25.64)
AA	11 (1.2)	8.23 ± 4.56	TCs:9 (81.82) Minoxidil: 2 (18.18)	0 (0)
Skin peeling	11 (1.2)	After loading dose	None	0 (0)
Parapsoriasis	3 (0.32)	18.7 ± 5.25	nb-UVB	3 (100)
Vitiligo	2 (0.21)	1.97 ± 2.67	nb-UVB + TCs	0 (0)

Abbreviations: AA, alopecia areata; ACD, allergic contact dermatitis; AIFF, alcohol-induced facial flushing; cAE, cutaneous adverse event; HN-D, head and neck dermatitis; nb-UVB, narrow-band ultraviolet B; SA, systemic antifungal; SC, systemic corticosteroid; TA, topical antifungal; TC, topical corticosteroid; TT, topical tacrolimus.

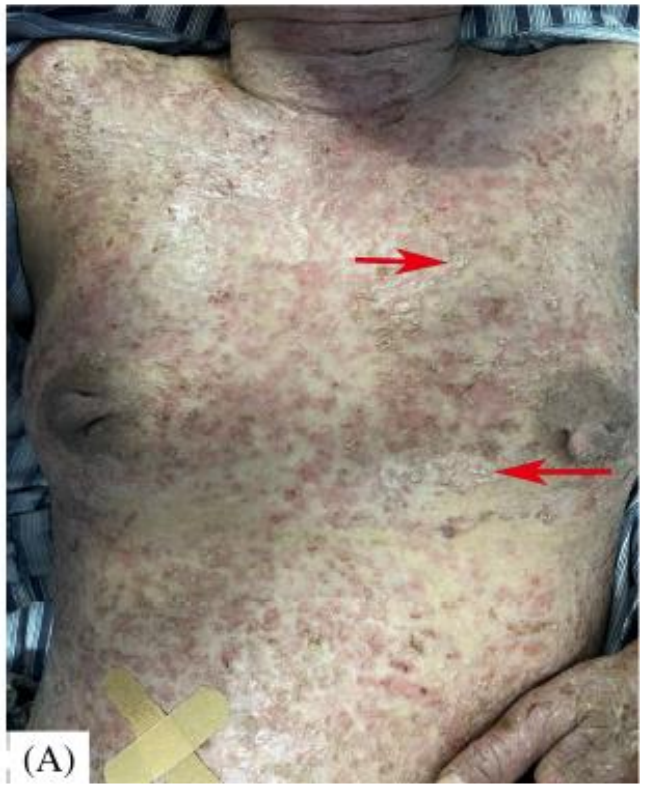
TABLE 3 Correlation of cAEs and clinical phenotype of atopic dermatitis.

Clinical phenotypes	HN-D	ACD	AIFF	Psoriasis	AA	Skin peeling	Parapso-riasis	Vitiligo	Total
Flexural	19	2	1	18	6	5		1	52
Generalized	12	3	2	11	3	4	3	1	39
Prurigo nodularis like	–	–	–	6	–	–	–	–	6
Head/neck dermatitis	40	1	–	–	–	–	–	–	41
Nummular	–	–	–	2	–	1	–	–	3
Flexural + head/neck + hand	2	–	–	–	2	1	–	–	5
Flexural + prurigo nodularis	–	–	–	2	–	–	–	–	2

Abbreviations: AA, alopecia areata; ACD, allergic contact dermatitis; AIFF, alcohol-induced facial; cAE, cutaneous adverse event; HN-D, head and neck dermatitis.

Dupilumab et induction de psoriasis

- Revue systématique littérature (2022):
  - 26 articles, identification de 47 cas
  - Apparition psoriasis 3.7 mois après introduction dupilumab
  - Phénotypes jusque là rapportés:
    - Plaques (zone bastion); KPP; érythrodermique; inversé; gouttes
  - Nécessité arrêt du dupilumab dans 48% des cas:
    - RC pso: 17%; RP pso: 67% ; sans impact sur pso: 17%



- **2023: Rapports de cas de psoriasis pustuleux, en particulier dans les populations asiatiques**

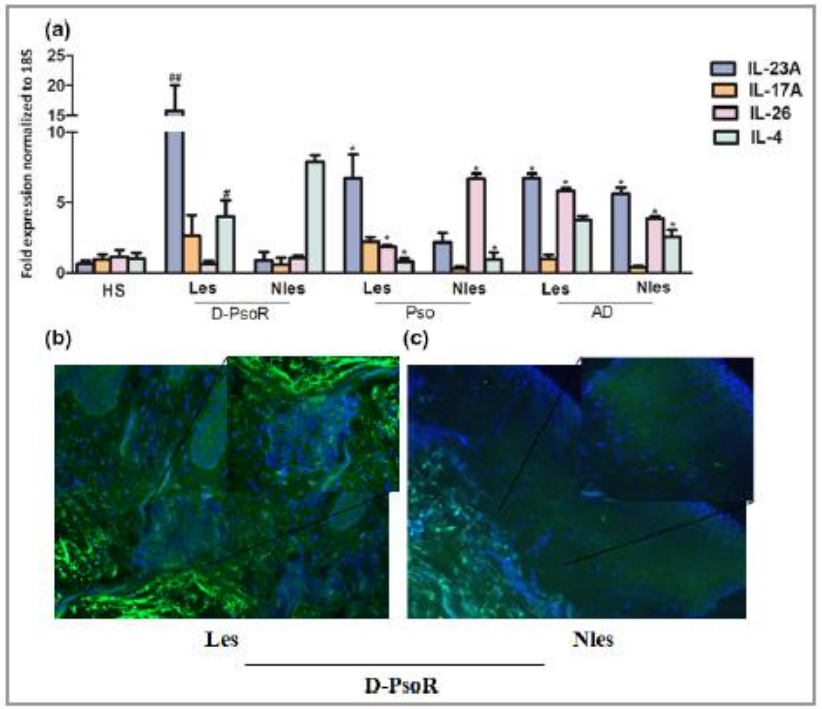
Brumfiel CM, et al. JAAD 2022; 86: 708-709
Jaulent L, et al. JEADV 2021

Liu L, et al. Clin Cosmet Investig Dermatol 2023
Zhong X, et al. Dermatol Ther 2022
Jia X, et al. J Drugs Dermatol 2022

British Journal of Dermatology (2021) **184**, pp340–373

Increased expression of interleukin-23A in lesional skin of patients with atopic dermatitis with psoriasiform reaction during dupilumab treatment

M. Napolitano,[1] G. Caiazzo,[2] G. Fabbrocini,[3] A. Balato,[2] R. Di Caprio,[3] E. Scala,[3] M. Scalvenzi[3] and C. Patruno[4]



J Invest Dermatol. 2023 May;143(5):711-721.e7. doi: 10.1016/j.jid.2022.10.015. Epub 2023 Jan 5.

IL-4/IL-13 Inhibitors for Atopic Dermatitis Induce Psoriatic Rash Transcriptionally Close to Pustular Psoriasis

Chloé Grolleau [1], Andreea Calugareanu [2], Sarah Demouche [1], Audrey Nosbaum [3], Delphine Staumont-Sallé [4], Hélène Aubert [5], Charles Cassius [1], Marie Jachiet [6], Anne Saussine [6], Martine Bagot [6], Hervé Bachelez [7], Maxime Battistella [8], Claire Hotz [9], Aurélie Du Thanh [10], Marie-Noëlle Crépy [11], David Bergerat [12], Marine Merandet [12], Rachel Onifarasoaniaina [13], Antonio Alberdi [14], Alexandre How-Kit [15], Jean-David Bouaziz [16], Hélène Le-Buanec [12]

Gene profiling avec confirmation transcriptomique et protéomique
sur 7 biopsies cutanées de pso induit sous dupi (contrôles: 4 PV, 4 HD, 4 DA)

Activation voie Th17/IL23, avec également expression importante IL-36
Forte décroissance voie Th2

Received: 13 June 2023 | Accepted: 12 July 2023
DOI: 10.1111/jdv.19351

JEADV

LETTER TO THE EDITOR

Successful treatment with tralokinumab in patients with atopic dermatitis and dupilumab-induced psoriasis

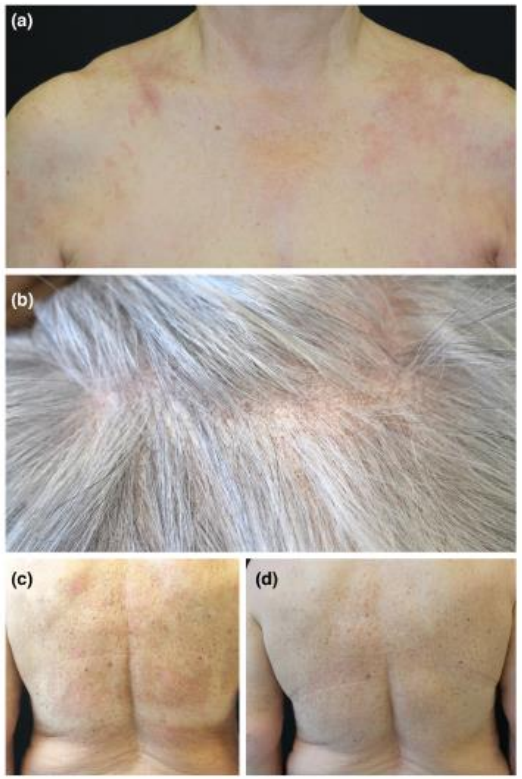


FIGURE 1 (a) Patient presentation with atopic dermatitis, (b) psoriatic plaques on the scalp during dupilumab therapy, (c) erythematous and scaling plaques on the trunk before starting tralokinumab and (d) resolution of the lesions after 2 months of tralokinumab.

JOURNAL OF DERMATOLOGICAL TREATMENT
2023, VOL. 34, NO. 1, 2258240
https://doi.org/10.1080/09546634.2023.2258240

Taylor & Francis
Taylor & Francis Group

CASE REPORT

Paradoxical tralokinumab-induced psoriasis in a patient with atopic dermatitis

Galina Balakirski[a#], Sven-Niklas Burmann[b#], Silke C. Hofmann[a] and Alexander Kreuter[b]

[a]Center for Dermatology, Allergology and Dermatosurgery, Helios University Hospital Wuppertal, University of Witten/Herdecke, Wuppertal, Germany; bDepartment of Dermatology, Venereology and Allergology, Helios St. Elisabeth Hospital Oberhausen, University of Witten/Herdecke, Oberhausen, Germany

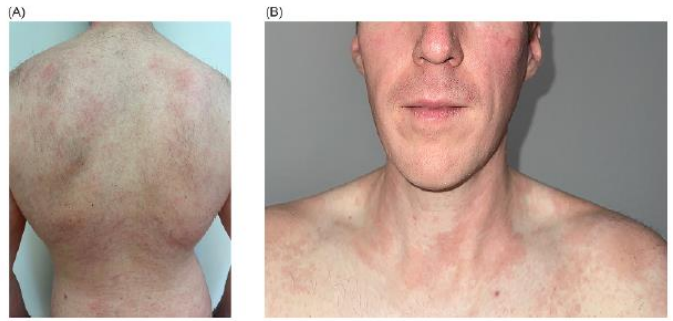


Figure 1. Clinical presentation of severe AD prior to the initiation of systemic therapy with erythematous, dry skin and scratch marks on the back (A) and neck (B). the SCORAD (SCORing atopic dermatitis) was 65.

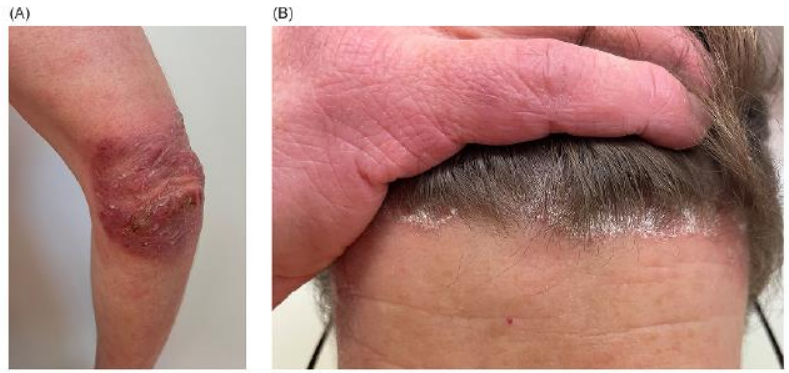


Figure 2. Clinical presentation of paradoxical tralokinumab-induced psoriasis with red, scaly plaques on the elbows (A) and erythematous patches at the hairline covered by silvery-white scales (B).

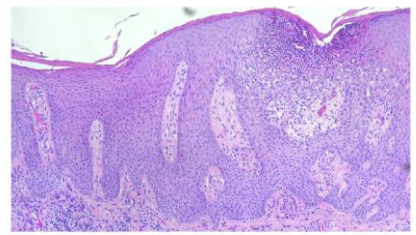


Figure 3. Histology of a skin biopsy from the lesion on the elbow with hyper- and parakeratosis, acanthosis, papillomatosis and subcorneal Munro's microabscess, that is typical for psoriasis. Hematoxylin-eosin staining, ×100.

- Arthralgies rapportées chez 5% des patients dans les essais cliniques, sans caractérisation

- **2023: Caractérisation rhumatisme inflammatoire apparaissant sous dupilumab**

Brumfiel CM, et al. JAAD 2022; 86: 708-709
Jaulent L, et al. JEADV 2021

Arthritis & Rheumatology
Vol. 0, No. 0, Month 2023, pp 1–5
DOI 10.1002/art.42558

American College of Rheumatology
Empowering Rheumatology Professionals

BRIEF REPORT

Characterization of a Musculoskeletal Syndrome of Enthesitis and Arthritis in Patients With Atopic Dermatitis Treated With Dupilumab, an Interleukin-4/13 Inhibitor

Catherine D. Hughes,[1*] Joseph Nathan,[1*] Libin Mathew,[2] Andrew E. Pink,[2] Richard T. Woolf,[2] Catherine Smith,[3] Bina Menon,[1†] and Bruce Kirkham[1†]

470 patients initiant dupilumab pour DA

Sur 36 patients adressés pour symptômatologie rhumatologique: 26, tous répondeurs à dupilumab, ont développé un **tableau proche d'un rhumatisme psoriasique, parfois sévère, avec enthésite, arthrite et ténosynovite** (5,5%), 17 semaines en moyenne après début.

Amélioration sous AINS, après réduction dose ou arrêt dupilumab, mais persistance symptômes sur plusieurs mois.

Pas de facteur prédictif identifié.

Table 1. Clinical characteristics and imaging results of 26 atopic dermatitis patients with subsequent musculoskeletal syndrome*

	Enthesitis†	Enthesitis and arthritis†	Arthritis	Enthesitis and tenosynovitis†	Sacroiliitis
Symptoms/clinical examination	12	8	3	3	4
Ultrasonography (n = 19)	9	5	2	1	–
Peripheral MRI (n = 7)	5	1	1	1	
Spine/SI joint MRI (n = 4)	–	–	–	–	1

* Values are the number of patients. MRI = magnetic resonance imaging; SI = sacroiliac.
† In patients diagnosed as having enthesitis, the most common sites were lateral epicondyle, Achilles, and patellar tendons.

Table 2. Long-term outcome of musculoskeletal symptoms relating to initial symptom severity and dupilumab dose changes or cessation*

	Resolution of symptoms			Persistent symptoms	
	No change in dupilumab dose	Dupilumab dose reduction	Dupilumab cessation	No change in dupilumab dose	Dupilumab cessation
Initial symptom severity					
Mild (n = 16)	9	4	3	–	–
Moderate (n = 6)	0	2	3	1	–
Severe (n = 4)	0	0	1	0	3

* Values are the number of patients among 26 total atopic dermatitis patients.

Dupilumab et induction de vitiligo

Received: 13 October 2022 | Accepted: 24 April 2023

DOI: 10.1111/jdv.19132

JEADV JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

LETTER TO THE EDITOR

Vitiligo induced by dupilumab treatment: A case series

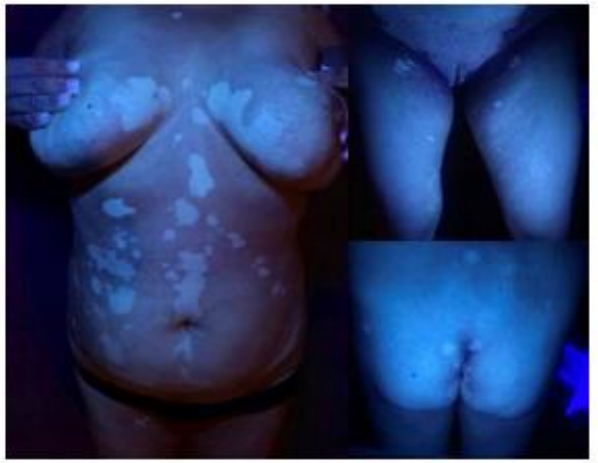


FIGURE 1 Patient 6. New depigmented macules and patches on bilateral breasts, chest, abdomen, proximal thighs and buttocks with confetti-like depigmentation, indicating rapidly progressing vitiligo.

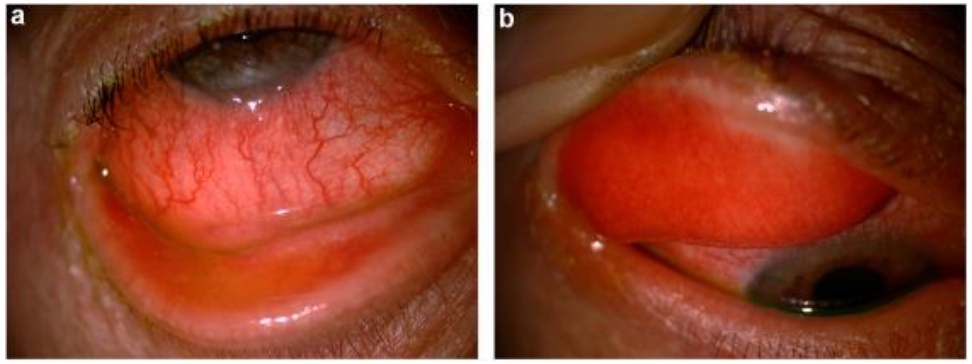
TABLE 1 Clinical characteristics of vitiligo patients.

Patient	Age	Gender	Skin type	Dupilumab indication	Duration from dupilumab initiation to vitiligo onset (months)	Vitiligo BSA (%)	Vitiligo type	Distribution of vitiligo	Dupilumab cessation	Previous history of vitiligo	Vitiligo outcome	Treatment
1	18	M	II	AD	2	3	NS	Bilateral cheeks, neck	Yes	No	Ongoing	Tacrolimus 0.1% ointment[a]
2	50	F	IV	AD	6	2	S	Right hairline, neck and chest	Yes	No	Resolution	Mometasone 0.1% ointment[a] and Nb-UVB
3	40	F	V	AD	5	8	NS	Hands and feet	No	No	Resolution	None
4	50	M	I	AD	3	1	NS	Hands, legs and feet	No	No	Resolution	Triamcinolone acetonide 0.1% ointment[a] and tacrolimus 0.1%[a]
5	18	F	IV	AD	4	6.25	NS	Pelvis, left leg and lower torso.	No	Yes	Resolution	Triamcinolone acetonide 0.1% ointment[a]
6	43	F	II	NP	1	15	NS	Face, bilateral breasts, chest, abdomen, bilateral forearms and proximal thighs	No	Yes	Stability	Betamethasone dipropionate 0.05% cream[a], tacrolimus 0.1% ointment[a] and Nb-UVB
7	52	M	IV	NP	3	2	NS	Forehead, glabella, nose and cheeks	No	Yes	Stability	Ruxolitinib 1.5% cream[a] and Nb-UVB

Abbreviations: AD, atopic dermatitis; F, female; M, male; nb-UVB, narrow-band ultraviolet B; NP, nasal polyposis; NS, non-segmental; S, segmental.

[a]Twice daily.

Dupilumab et manifestations ophtalmologiques



Données méta analyse études et vie réelle estiment la survenue d'une blépharoconjonctivite chez 26,1% des patients DA sous dupilumab (*vs* 8% sous placebo)

- Facteurs de risque de développer une BC sous dupilumab =?

Sévérité de la DA? Atteinte oculaire pré existante? Hyperéosinophilie? IgE élévés?

- Risque inférieur sous anti-IL-13 (tralokinumab, lebrikizumab)?

- Intérêt de switcher du dupilumab vers un anti-IL-13 quand BC sévère nécessitant arrêt dupilumab?

Ou Z, et al. Int Immunopharmacol 2018; 54: 303-10
Akinlade B, et al. Br J Dermatol 2019; 181: 459-73

Received: 1 September 2022 | Accepted: 5 January 2023
DOI: 10.1111/jdv.18932

ORIGINAL ARTICLE

JEADV

Multicenter prospective observational study of dupilumab-induced ocular events in atopic dermatitis patients

Ingrid Costedoat[1] | Martin Wallaert[2] | Aurelie Gaultier[3] | Robin Vasseur[2] | Clelia Vanhaecke[4] | Manuelle Viguier[4] | Charles Cordelette[5] | Alexandre Denoyer[5] | Marie-Christine Ferrier le Bouëdec[6] | Adrien Coutu[6] | Marie Lamiaux[7] | Thi Ha Châu Tran[7] | Jean Philippe Lacour[8] | Valerie Elmaleh[8] | Florence Tetart[9] | Julie Gueudry[9] | Marie Tauber[10] | Francoise Giordano-Labadie[10] | Myriam Cassagne[11] | Audrey Nosbaum[12,13] | Coralie Ouilhon[12,13] | Marie Jachiet[14] | Ramin Tadayoni[15] | Frederic Dezoteux[16] | Delphine Staumont-Salle[16] | Julien Bouleau[17] | Pierre Labalette[17] | Serge Doan[18,19,20] | Angele Soria[18,19,20] | Bruno Mortemousque[1] | Julien Seneschal[1] | Sebastien Barbarot[2] | on behalf of the FRench Atopic DErmatitis Network from the Groupe de Recherche sur l'Eczema Atopique (GREAT), France

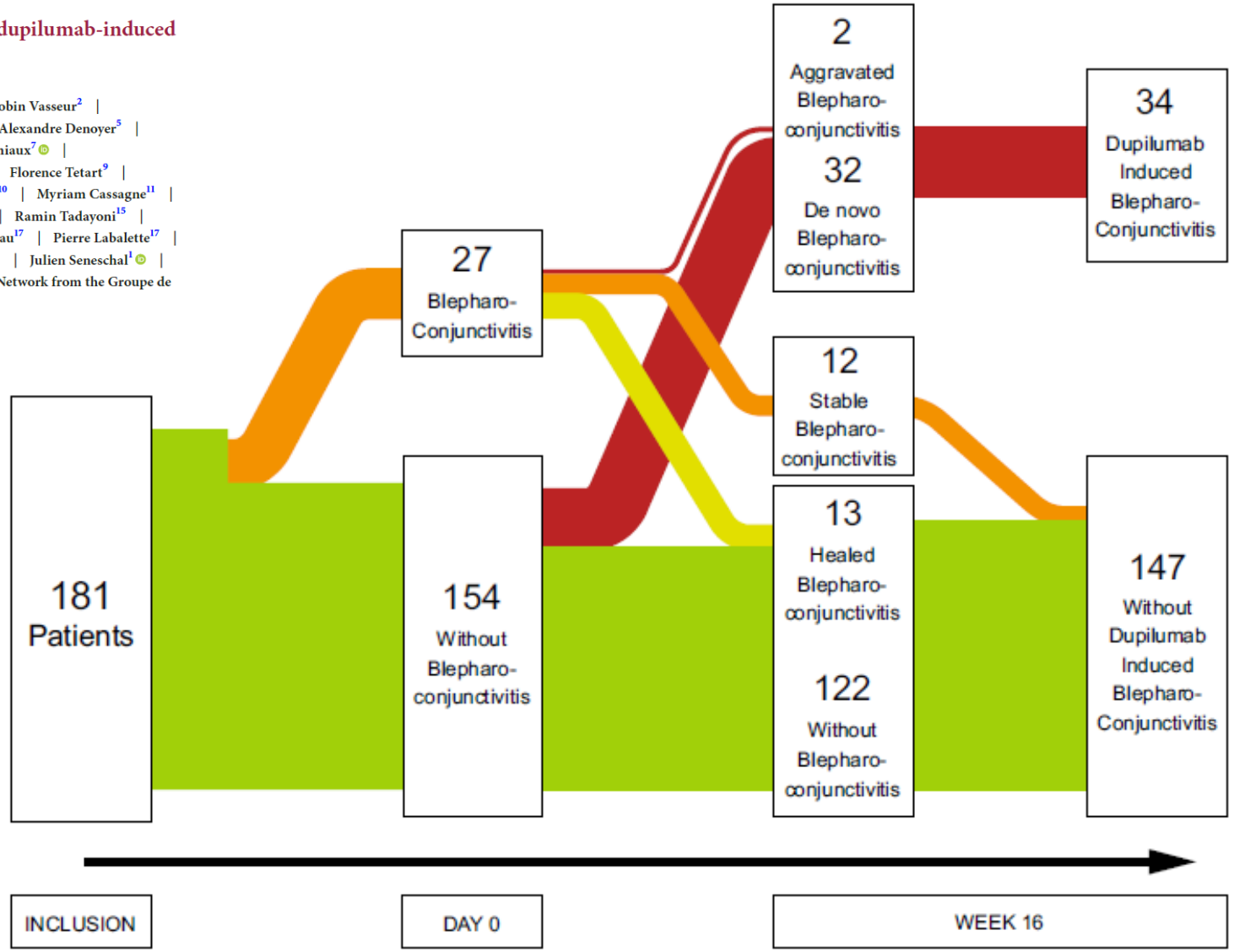


FIGURE 2 Clinical course of conjunctivitis between inclusion and W16.

18,7% des patients avec blépharoconjonctivite à S16
Modérée : 79,4% des cas
Sévère dans 14,7%

Costedoat I, et al. JEADV 2023; 37: 1056-1063

Trois facteurs de risque indépendants identifiés de développer une atteinte ophtalmologique dans la DA sous dupilumab

TABLE 3 Multivariate analysis of factors associated with the occurrence of dupilumab-induced blepharoconjunctivitis.

Risk factor	Patients without blepharoconjunctivitis ($n = 147$)	Patients with blepharoconjunctivitis ($n = 34$)	p	OR
AD phenotypes at inclusion				
Head and neck involvement	22 (14.97%)	10 (29.41%)	0.004	7.254 [1.938–30.07]
Erythroderma	24 (16.33%)	12 (35.29%)	0.007	5.635 [1.635–21.50]
Dry eye disease at inclusion	43 (30.71%)	17 (50.00%)	0.031	3.851 [3.158–13.90]

Pas d'association avec une atteinte ophtalmologique préalable quelle qu'elle soit+++

Une atteinte ophalmologique atopique ne doit pas restreindre l'initiation du dupilumab chez ces patients

Costedoat I, et al. JEADV 2023; 37: 1056-1063

Incidence of conjunctivitis adverse event in patients treated with biologics for atopic dermatitis: A systematic review and meta-analysis

Alraddadi R, et al. J Am Acad Dermatol 2023; 13:46-7

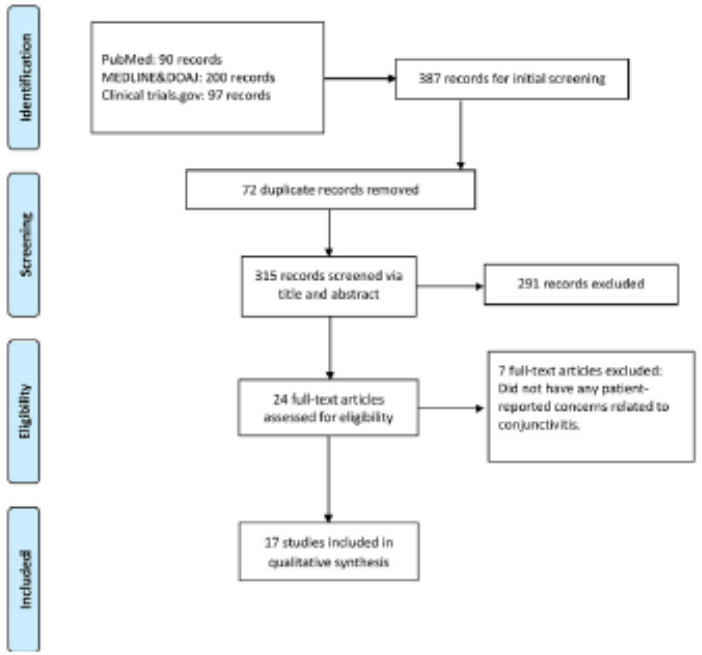


Fig 1. Study flowchart as per the preferred reporting items for systematic reviews and meta-analyses criteria.

5830 patients

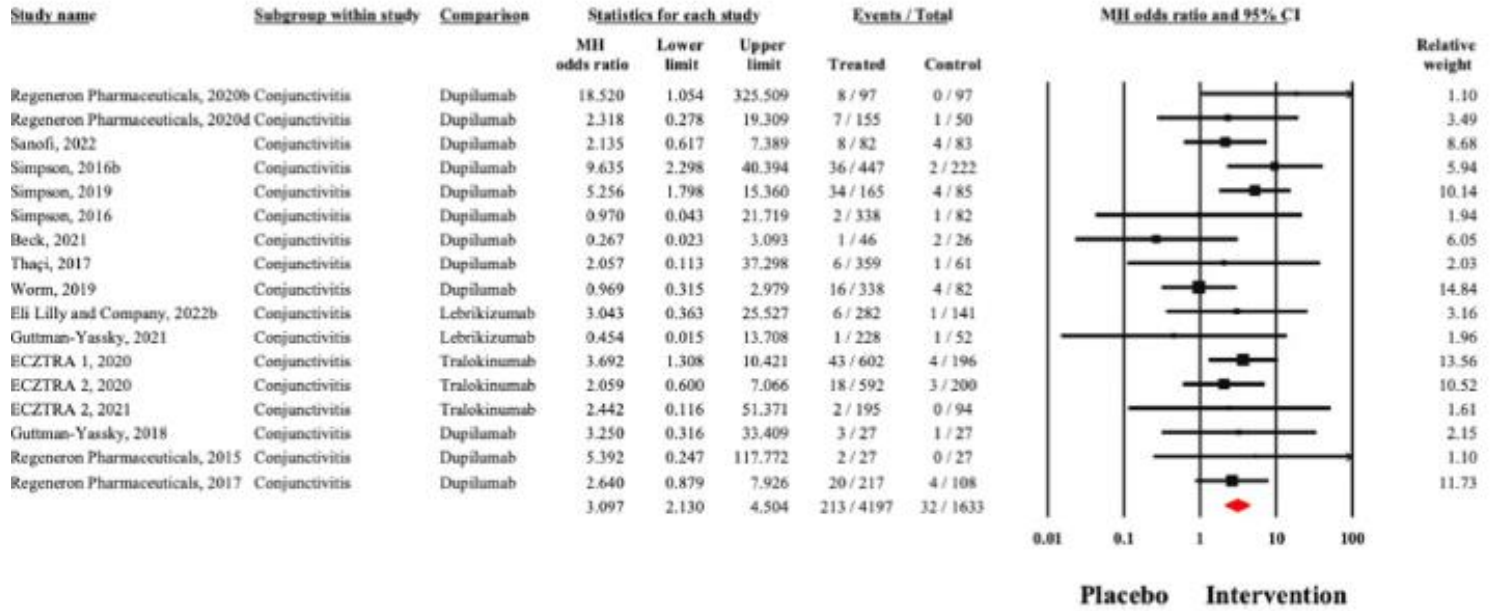


Fig 2. Forest plot presenting pooled effect size incidence of conjunctivitis adverse event with biologic therapies in atopic dermatitis.

OR (poolé): 3,11 (IC95%, 2,13-4,5)

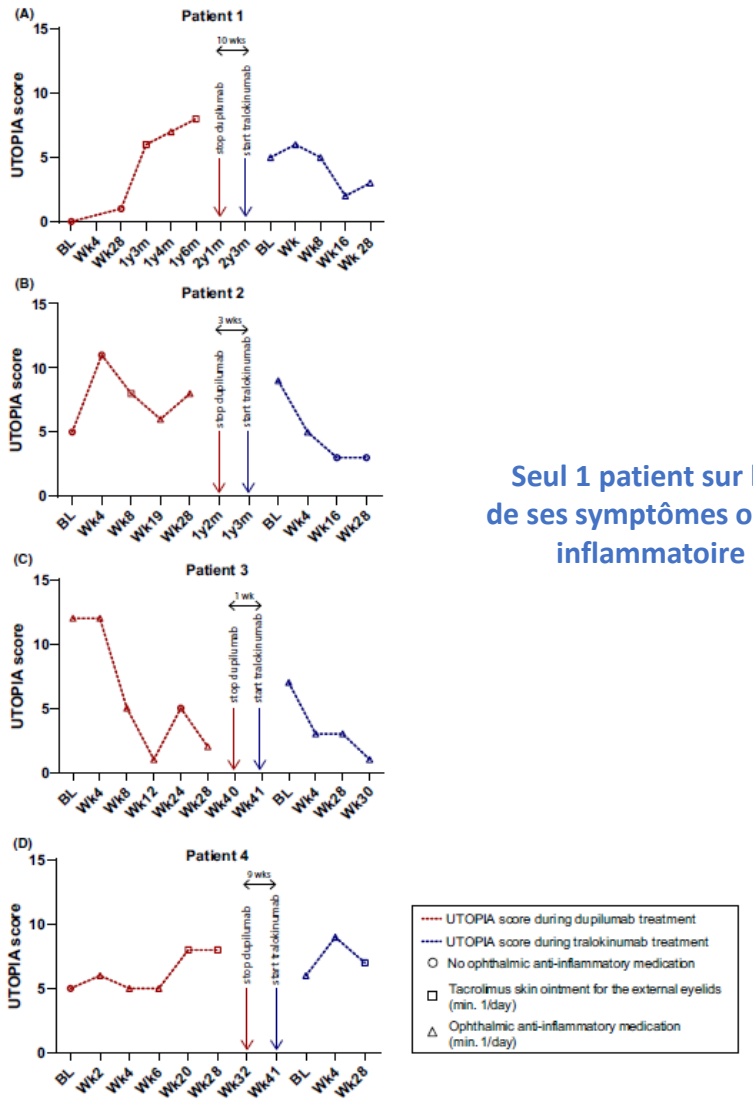
Pas de différence d'incidence de conjonctivite entre dupilumab (anti IL4/IL13), tralokinumab et lebrikizumab (anti IL13)

Received: 11 January 2023 | Revised: 22 February 2023 | Accepted: 24 February 2023
DOI: 10.1111/cea.14305

Switching from dupilumab to tralokinumab in atopic dermatitis patients with ocular surface disease: Preliminary case series

TABLE 1 Patient characteristics during dupilumab and tralokinumab treatment at baseline and week 28.

	Dupilumab treatment		Tralokinumab treatment	
	Baseline	Week 28	Baseline	Week 28
Patient 1, ♀, age 27 years				
UTOPIA score	0	1[a]	5	3
EASI score	16.7	2.4	3.2	3.8
Number of symptoms	0/6	1/6	2/6	4/6
Ophthalmic medication use	None	Tacrolimus skin ointment for external eyelids as needed	• Hydrocortisone eye drops 1/day ODS • Lubricant eye drops as needed	• Hydrocortisone eye drops 1/day ODS • Lubricant eye drops as needed
Patient 2, ♂, age 52 years				
UTOPIA score	5	8	9	3
EASI score	26.7	4.2	6.0	7.1
Number of symptoms	3/6	4/6	5/6	2/6
Ophthalmic medication use	None	• Standard treatment[b] • Hydrocortisone eye drops 2/day ODS	• Dexamethasone eye drops 3/day ODS • Ketotifen eye drops 2/day ODS	Lubricant eye ointment as needed
Patient 3, ♂, age 71 years				
UTOPIA score	12	2	7	3
EASI score	26.5	0.9	0.5	1.2
Number of symptoms	5/6	1/6	0/6	1/6
Ophthalmic medication use	Hydrocortisone, oxytetracycline and polymyxine B eye ointment 1/day ODS	Dexamethasone eye drops 2/day ODS	Dexamethasone eye drops 2/day ODS	Dexamethasone eye drops 1/day ODS
Patient 4, ♀, age 28 years				
UTOPIA score	5	8	6	7
EASI score	2.1[c]	6.4	7.7	8.1
Number of symptoms	4/6	5/6	4/6	3/6
Ophthalmic medication use	Lubricant eye ointment ante noctem	Standard treatment[b]	• Standard treatment[b] • Hydrocortisone, oxytetracycline and polymyxine B eye ointment 2/day ODS	Standard treatment[b]



Seul 1 patient sur les 4 obtient à la fois une diminution de ses symptômes oculaires et une amélioration d'un score inflammatoire après switch pour le tralokinumab

Achten R, et al. Clin Exp Allergy 2023; 53: 586-9

Dupilumab, grossesse et allaitement

Received: 2 February 2023 | Accepted: 26 April 2023
DOI: 10.1111/jdv.19165

LETTER TO THE EDITOR

JEADV

Dupilumab for atopic dermatitis during pregnancy and breastfeeding: Clinical experience in 13 patients

- Dupilumab: IgG4, passage barrière placentaire 2ème et 3ème trimestre, mais passage minimal dans lait et dégradation attendue par sucs gastriques.
- Pas de toxicité identifiée sur modèles animaux. Etude pharmacovigilance (Vigibase): pas de signal.

- **Etude rétrospective monocentrique espagnole sur 11 grossesses et 2 allaitements:**
  - Exposition pendant grossesse: 6.8 +/_2.9 mois
    - Soit introduit pendant grossesse, soit maintenu pendant toute la grossesse ou arrêt après le premier trimestre
    - 10 naissances à terme avec poids naissance normal
    - 1 naissance gémellaire prématurée, non compliquée
    - Pas de fausse couche
    - **Aucun enfant n'a développé de DA!**
  - Exposition pendant allaitement: 11.5 +/_3.2 mois

Vestergaard C, et al. JEADV 2019
Khamisy-Farah R, et al. Eur Rev Med Pharmacol Sci 2021

Traitements systémiques de la dermatite atopique en cours de développement

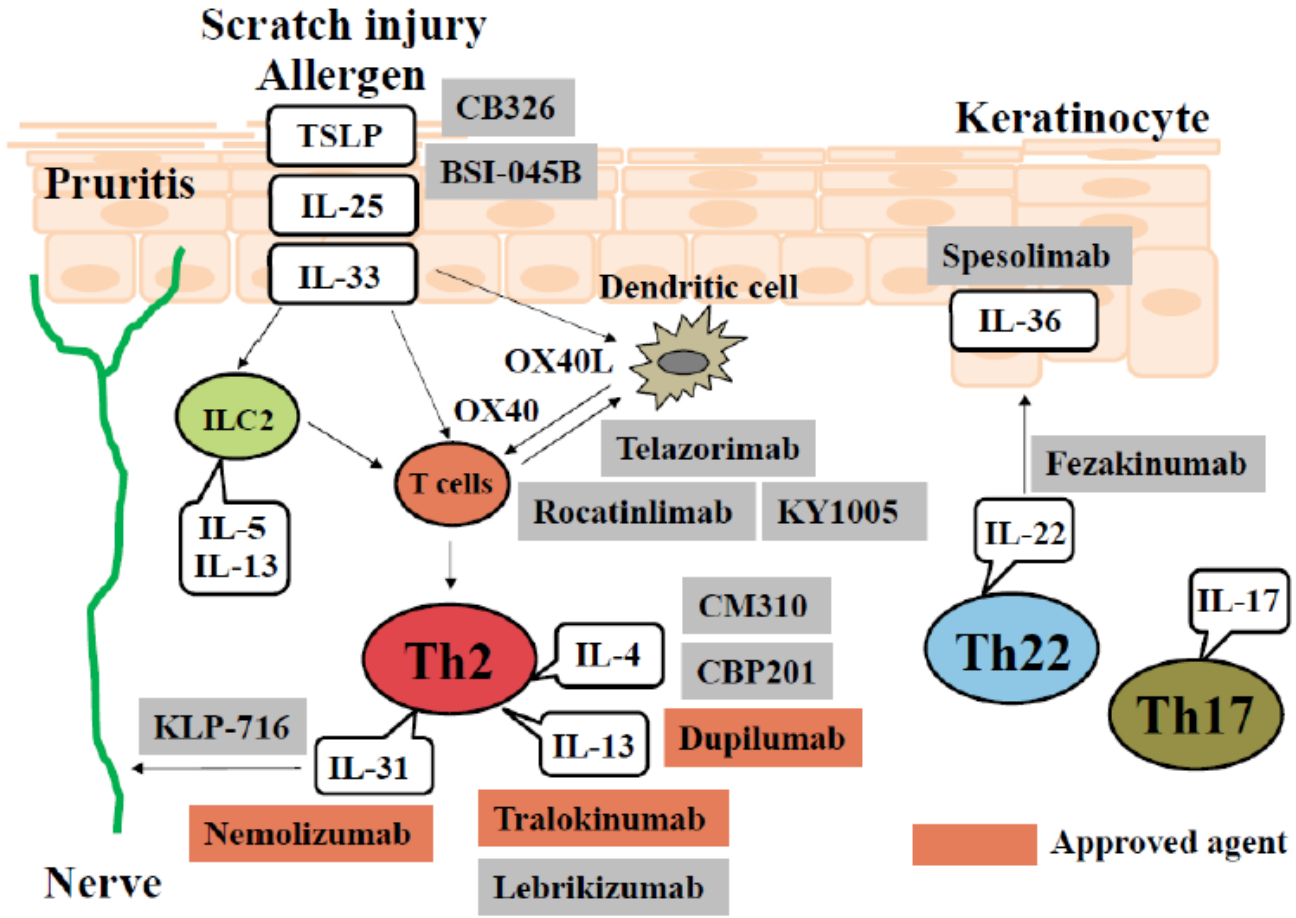
biomedicines

MDPI

Review

Novel Therapeutic Targets for the Treatment of Atopic Dermatitis

Gaku Tsuji [1,2,*], Kazuhiko Yamamura [1,2], Koji Kawamura [2], Makiko Kido-Nakahara [2], Takamichi Ito [2] and Takeshi Nakahara [1,2]



Cible	DCI	Phases achevées
IL13	lebrikizumab	III
IL31	nemolizumab	III
JAKi	gusacitinib	II
TLSP	tezepelumab	II
IL22	fezakinumab	II
OX-40	telazorlimab	II
OX-40	rocatinlimab	II
OX-40L	amlitelimab	II

Guttman-Yassky et al. Lancet 2023 (rocatinlimab)
Weidinger S et al. Br J Dermatol 2023 (amlitelimab)

Conclusions

- Le champs thérapeutique de la DA continue à s'agrandir avec l'arrivée prochaine d'un anti-IL31 (nemolizumab), d'un autre anti IL-13 (lebrikizumab), et à terme d'une nouvelle classe de biothérapie ciblant axe Ox40-Ox40L.

- L'efficacité inter et intra classe est très différente d'une molécule à l'autre, et chaque classe thérapeutique a un profil de toxicité propre.

- Comme précédemment observé avec les anti TNF, des effets secondaires finalement fréquents n'avaient pas été rapportés ou caractérisés lors des essais (ex: psoriasis et rhumatisme psoriasique sous dupilumab).

- Enjeu actuel: choisir la bonne molécule pour le bon patient.